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THE ETIOLOGY OF BREAST CANCER, RISK FACTORS, PROTECTION FACTORS

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Abstract

The present paper aims to support the importance of knowledge of risk factors, of protection factors in the etiology of breast cancer and their influence in order to improve the quality of life of patients and increase healing chances.

Key words: breast cancer, etiology, risk factors, protection factors, genes, estrogen, quality of life.

INTRODUCTION

Breast cancer is a condition with complex implications in evolution over the quality of life, it is characterized by an evolution with extremely high variability from one patient to another. It is admitted today that most breast cancers are dependent on hormonal factors that influence changes in breast-level from birth to advanced ages.

MATERIAL AND METHOD

Knowledge has been analyzed until the present time of the etiology of breast cancer. The influence of hormonal factors, geneticsinherintances, premalignant lesions, cellular mutations of normal cells, suppressor genes, but also the influence of external factors are important to be known by professionals and patients, to be able to have tailored interventions.

RESULTS AND DISCUSSION

Certain aspects, such as protection factors, may change the likelihood of a person developing breast cancer or not, but there are also risk factors with which they cannot fight, age, gender, genetic inheritance.

1.Epidemiology

Breast cancer is a major public health problem, having an incidence in the European Union and a high mortality. In 2006, the annual incidence adjusted by age of breast cancer in the European Union (data from 25 countries) was 110,3/100.000 women, and the annual mortality through breast cancer was 25/100.000 women[1]. Breast cancer is the most common neoplastic disorder in women, in our country, with a number of 4200 newly diagnosed cases and 2500 deaths per year[2]. Although there is an increase in the number of new cases the mortality rate remains constant in the last 20 years[3], more than half of the diseased are diagnosed in advanced stages and therefore the therapeutic costs are high and the results less good.

2. Etiology

The breast is an integral part of the female reproductive system with a role in breastfeeding, consisting of glandular tissue, fatty tissue and fibrome tissue. The breast is considered an interactive community in which the cells of the ducts and lobules interact and influence the fibrome tissue, the blood vessels and the surrounding fat, the most important component being the lactiferous ducts system, responsible for Lactation. The lactiferous ducts unite inside the breast in a common duct that opens up to the skin, being between 6 and 9 main ducts that open at the nipple level. At the end of the ductal system are lobules. Inside, the ductal system is lined with a layer of small cells that suffer changes, which appear to be involved in the appearance of breast cancer. The cells of adipose tissue that develop around canalicules and lobules are also specialized cells, correlated with ductal cells and lobular, influencing each other. The dysfunctions that accur at the correlation level between these cells create conditions for the development and growth of breast cancer.

At birth the breast is not fully developed, so in puberty when it develops it needs stem cells that are able to transform into another type of ductal cells or lobular, they will intervene in the period when the breast produces milk and when the breastfeeding period ends, these cells could become mutants, triggering cancer. During the monthly menstrual cycle, changes are produced in the ductal and lobular system, as well as the surrounding tissue, changes being influenced by the hormonal level.Breast transformation during lactation is coordinated by the level of estrogen,

1 Clinical recommendations for breast cancer, ESMO recommendations for diagnosis, treatment and follow-up, Annals of Oncology 20 (Supplement 4): iv10 – Iv14, 2009, doi: 10.1093/annonc/mdp114

2 Guilezan N, Diagnostic and Treatment guide, Oncology Committee

3 Ghilezan N, Vitoc C, Găfainanu MR, et al. Therapeutic methods and results in breast cancer, Romania 1990-1992. Multicentre Study of SRRO. Radioter & Oncol Med 1996; II, 3-4:1-7.

progesterone, prolactin and oxytocin. During pregnancy, the maturation of the lobules occurs, the type 4 mature lobulum is maintained during pregnancy and during lactation. Mature lobules are less vulnerable to cancer, immature structures being considered to be more susceptible to carcinogenesis, which would explain why early age pregnancies decrease the risk of breast cancer. At menopause fluctuations in estrogen levels and decreasing the level of progesterone attract a number of specific changes in which the mammary gland is involved. Women who present a higher level of estrogen and testosterone have a higher vulnerability towards breast cancer.

To develop and to thrive any cancer needs two fundamental elements: the first is a cell that for some reason, either hereditary or carcinotic, has undergone a mutation of an important part of the DNA, mutation that modifies its potential behavior; the second element is represented by the neighbouring cells that can positively or negatively influence cells with mutations, otherwise said the cancer is caused by a combination of genes altered by carcinogens and a favorable environment for growth and propagation.

The oncogenes and suppressive genes are involved in the development of cells and only if mutations are produced they become carcinogenic. One of the proto-oncogenes is related to the epidermala EGFR growth factor, useful during puberty when important development-related transformations are happening. One such factor is factor is the epidermala growth factor 2 called HER-2/neu, or erB-B2, which may undergo a change in the type of amplification that can cause an accelerated growth and multiplication of a malignant cell in the vicinity.

The tempering of oncogenes and proto-oncogenes is performed by tumor suppressant genes that act as brakes in cell multiplication with mutations. Such a suppressant gene is p53 that prevents cells with an AND that has undergone mutations to divide. If the p53 gene is compromised the division of cells with mutations of AND it cannot be stopped. Molecular biology has highlighted two mutations occurring in BRCA 1 and BRCA 2 suppression genes, mutations that are responsible for the occurrence of hereditary breast cancer.

As with other localization of cancer, and in malignant tumors of the breast local dissemination (in the breast) is done by invasion, tumor cells infiltrating tissues along galactose canals and fascial septures to the surrounding fat, which gives The tumor's irregular appearance, starry, a special form of cutaneous infiltration is the "patting nodules", small tumor formations located in the dermal lymph nodes of the breast or exceeding the boundaries of the organ[4]. It is admitted that until the clinical discovery (1-2

4 Bălanescu I., Blidaru AL., Breast cancer, Angelescu N., Surgical Pathology Treaty, vol. 1

cm) or imaging (a few mm) of a breast cancer can pass several years, a breast cancer being curable when the diagnosis is put into the preclinical phases of its evolution[5]. However, approximately 7% of breast cancers have a very rapid evolution[6], the disease is generalized in a few months. The local extension process is made either to the fascia of the pectoral muscle and the thoracal wall to which it can be fixed, either to the skin it invents, the characteristic signs of orange peel, edema, ulceration with superinfection and hemorrhage[7].

3. Risk factors

a) Female sex, the most important risk factor is even female sex.
b) Age: the more we get older, the more our cells divide and more DNA errors can occur. Three-quarters of breast cancers are diagnosed after menopause. The risk of developing a breast cancer is almost 1:20,000 at the age of 25, but up to the age of 80, the risk reaches 1:8.
c) Hormonal factors

Estrogen: the risk of developing a breast cancer increases the exposure to higher amounts of long time me to this hormone. The risk is increased in women who have had their first menstruation at less than 12 years of age or in women in whose menopause has been installed at the age of 55 years or older. Studies have shown that women who have higher concentrations of estrogen in post-menopausal blood have a twice greater risk than women who have lower estrogen concentrations. Most major risk factors for breast cancer can actually be explained by their effect on hormones. Hormone replacement therapy is sometimes prescribed to relieve the symptoms associated with menopause. There are two main types: combination therapy, with estrogen and progesterone, and estrogen-only therapy. Multiple studies have shown that post-menopausal hormonal subtitution therapy increases the risk of developing breast cancer, especially the combination of estrogen and progesterone. The largest clinical trials in this field were the "Women's Health Initiative", conducted in the United States of America, and "Million Women Study"-The study of a million of women-in the UK.

d) Family history: Theoretically, if the mother or sister had breast cancer, a woman's risk of getting sick is double. However, more than 8 out of 10 women who have had cases of breast cancer in the family will never have this disease. This risk can be determined by an

5Rochet Y. - Cancer Gynecologioques et Mammaires, Flammarion medecine sciences, 1986.

6 Angelescu N., treatment of Surgical Pathology, vol. 1, Medical Publishing House, Bucharest, 2003

7 Angelescu N., treatment of Surgical Pathology, vol. 1, Medical Publishing House, Bucharest, 2003

inherited defect gene. There are two main genes involved in the genetic forms of breast cancer are BRCA1 and BRCA2. The risk of developing a breast cancer in people who have inherited one of these two "defects" genes varies between 45% – 85%, the direct inheritance of specific genetic defects such as mutations in the BRCA1 gene occurring in chromosome 17 (Locus 17q21), in 5-10% of all breast cancers[8], the altered transmission of the BRCA 2 gene competes in the occurrence of breast cancer and especially in the occurrence of ovarian cancer[9]. This risk can be reduced by prophylactic surgery, with careful genetic evaluation and counselling, prophylactical treatment, careful supervision through mammograms and breast MRI.

Genes that accelerate cell division are called oncogenes. Proto-oncogenes are genes that normally help cells grow. When a proto-oncogenic mutates (changes) or if there are too many copies of it, it becomes an unhealthy gene, which can be activated permanently, so the cell grows uncontrolled, becomes oncogenic and can transform normal mammalar epithelial cell into a malignant one.

Tumor suppressant genes are normal genes that slow down cell division, repair DNA errors or intervene in apoptosis. When the tumor suppressant genes do not work properly, cells can grow uncontrolled which can lead to cancer. RB suppressant genes, NM23, p53, inhibit the proliferation process of tumor cells[10]. Certain mutations in DNA that "activate" oncogenes or "disable" tumor suppression genes can cause normal breast cells to become cancerous.

Hereditary transmission of breast cancer is very much discussed. It is acknowledged today that this issue should be seen from 2 points of view: the family aggregation syndrome involving a genetic predisposition dependent on interactions with the environment, family history of the Li-Fraumeni syndrome, the Cowdensyndrome, the Muir syndrome, ataxia-teleangiectasy and ovarian cancer, increase the possibility of developing breast cancer.

Inherited genetic mutations

Normal breast cells can become cancerous due to DNA changes (mutations). Some mutations in the DNA are inherited, mutations exist in every cell in the body and can substantially increase the risk of developing

8 Bălanescu I., Anghel Rodica- Breast cancer; Surgical Pathology; Under the redaction of Angelescu N., Celsius Publishing House, Bucharest,1997.

9 Dickson R.B. Lippman M.E. - Advances in Cellular and Molecular Biology of Breast Cancer, Boston, 1996.

10 Angelescu N., Treatise on Surgical Pathology, vol. 1, Medical Publishing House, Bucharest, 2003

certain cancers. BRCA genes (BRCA1 and BRCA2) are tumour suppressant genes. Modification of one of these genes can be inherited familial. Genetic tests can identify some women who have inherited mutations in tumour suppression genes BRCA1 or BRCA2 (rarely other genes like PTEN or TP53). Mutations of tumor suppressant genes as BRCA genes are considered to have a "high degree of penetration" because they often lead to cancer. The genes involved can affect issues such as hormonal levels and metabolism.

Acquired genetic changes

These acquired mutations of oncogenes and / or tumor suppressor genes may derive from other factors, such as radiation or chemicals that cause cancer. Tests to detect acquired genetic changes can help physicians more accurately formulate the prognosis for breast cancer. For example, tests can identify those cases where the cancer cells have too many copies of the HER2 oncogene, cancers that tend to be more aggressive, but drugs that specifically target these cancers have been developed. The risk of developing breast cancer increases as it progresses in age. Breast cancer is more common among women over the age of 50, who have gone through menopause, 8 out of 10 breast cancer cases occur in women over 50.

e) Personal history of breast cancer: a woman who has had breast cancer has a higher risk of developing another cancer in the same breast or in the other.
f) Personal history of other diseases: breast cancer occurs more frequently in women who have previously suffered from other cancers: Hodgkin's lymphoma (especially at young ages and if treated by radiation), malignant melanoma, lung cancer, colorectal cancer, uterine body cancer, lymphocytic leukemia chronic.
g) Benign breast disease: most benign (non-cancerous) breast diseases do not increase the risk of cancer. Depending on how dangerous they are, these diseases are divided into three categories:
    i. Non-proliferative lesions - in which cells do not divide, do not grow, include: mastitis, fibrocystic mastopathy, ductal ectasia, steatonecrosis, single papilloma, lipomas.
    ii. Proliferative lesions without atypia - the cells divide in excess, but they are normal, include: ductal hyperplasia, fibroadenomas, sclerosing adenosis, papillomatosis.
    iii. Proliferative lesions with atypia - the cells divide excessively, and some no longer look normal, significantly increase the risk of cancer (~ 3 times). They include atypical lobular hyperlasia, atypical ductal hyperplasia, in situ lobular carcinoma. In situ lobular carcinoma is a disease in which abnormal cells grow, the presence of in situ lobular

carcinoma indicates an increased risk of developing cancer in either breast[11]. In situ ductal carcinoma, on the other hand, is a form of early cancer that can turn into invasive cancer. However, only one in 6 women with lobular or ductal carcinoma in situ will develop breast cancer within 10 years.

h) Density of the breasts: some women have more glandular and fibrous tissue, and their breasts have a higher density on mammograms, with more mammary cells present and the risk of developing cancer is increased up to 2 times.
i) Smoking and alcohol consumption: alcohol consumption slightly increases the risk of developing breast cancer, smoking increases the risk, especially in women who smoke from a young age.
j) Height and weight: older women have a higher risk of developing breast cancer, women who had a higher birth weight have a higher risk of breast cancer before menopause. Overweight or postmenopausal obese women also have an increased risk, overweight women also have increased levels of insulin in the blood, another hormone that seems to increase the risk.
k) Social environment: women in Western countries may have an increased risk of developing breast cancer.
l) X-ray exposure: exposure to radiation increases the risk of many cancers, chest radiotherapy for the treatment of Hodgkin's lymphoma, especially if done in childhood, can increase the risk of breast cancer.
m) Assumed and unproven risk factors: trauma to the breast, antiperspirants, abortions, stress (breast tumors are not proven to be its consequences), breast implants (silicone implants most commonly associated with a rare form - lymphoma with large anaplastic cells), working in night shifts (slightly increased risk).

4. PROTECTION FACTORS

As risk factors increase the likelihood of someone getting sick of a certain disease, there are also protective factors that can help to lower this probability.

a. Pregnancy is a protection factor. Breast cancer occurs more frequently in women who do not have children-or who bear the first child at an older age, a woman who has the first child over 35 years has a risk of 5 times higher to develop this disease against a woman who has the first child at 18 years.

11Bălanescu I., Blidaru AL., breast cancer, Angelescu N., treatment of Surgical Pathology, vol. 1, Medical publishing house Bucharest, 2001.

b. Breastfeeding – breastfeeding women have a lower risk of developing breast cancer, especially if they had the first child at a younger age.
c. Physical activity-studies show that the movement (for half an hour, 5 times a week) decreases the risk of breast cancer by 20% (one-fifth), even a few walks at a more rapid pace may decrease the risk.
d. Nutrition- it is estimated that we could avoid almost one in ten cases of cancer just by changing the diet. There are some conclusions: sugars, carbohydrates, fats especially saturated fat after menopause, can double the risk, lactates through their calcium content has a protective effect, fibers, fruits and vegetables contain many antoxidants, prevent damage to cells, soybeans and phytoestrogens, seem to slightly decrease the risk.

CONCLUSIONS

Breast cancer is characterized by an evolution of extremely high variability from one patient to another. It is admitted today that most breast cancers are dependent on hormonal factors that influence changes in breast-level from birth to advanced ages. Certain aspects, such as protection factors, may change the likelihood of a person developing breast cancer or not, but there are also risk factors with which they cannot fight, age, gender, genetic inheritance.

REFERENCES

1. Angelescu N., treatment of Surgical Pathology, vol. 1, Medical Publishing House, Bucharest, 2003.
2. Bălanescu I., Anghel Rodica- Breast cancer; Surgical Pathology; Under the redaction of Angelescu N., Celsius Publishing House, Bucharest,1997.
3. Bălanescu I., Blidaru AL., Breast cancer, Angelescu N., Surgical Pathology Treaty, vol. 1, Medical Publishing house Bucharest, 2001
4. Clinical recommendations for breast cancer, ESMO recommendations for diagnosis, treatment and follow-up, Annals of Oncology 20 (Supplement 4): iv10 – Iv14, 2009, doi: 10.1093/annonc/mdp114.
5. Dickson R.B. Lippman M.E. - Advances in Cellular and Molecular Biology of Breast Cancer, Boston, 1996.
6. Ghilezan N, Diagnostic and Treatment guide, Oncology Committee.
7. Ghilezan N, Vitoc C, Găfainanu MR, et al. Therapeutic methods and results in breast cancer, Romania 1990-1992. Multicentre Study of SRRO. Radioter & Oncol Med 1996; II, 3-4:1-7.
8. Rochet Y. - Cancer Gynecologioques et Mammaires, Flammarion medecine sciences, 1986.